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<p>(21) International Application Number: <b>PCT/US94/04193</b></p> <p>(22) International Filing Date: <b>15 April 1994 (15.04.94)</b></p> <p>(30) Priority Data:  08/049,818                      20 April 1993 (20.04.93)                      <b>US</b></p> <p>(60) Parent Application or Grant  (63) Related by Continuation  <b>US</b>    08/049,818 (CIP)  Filed on    20 April 1993 (20.04.93)</p> <p>(71) Applicant (for all designated States except US): <b>MEDCHEM PRODUCTS, INC. [US/US]; 232 Cummings Park, Woburn, MA 01801 (US).</b></p> <p>(72) Inventors; and  (75) Inventors/Applicants (for US only): <b>FERDMAN, Ariel, G. [US/US]; 12 Hillside Avenue, Melrose, MA 02176 (US). PINSKY, Vladimir, J. [US/US]; 10 Lake Shore Terrace, No. 4, Brighton, MA 02135 (US).</b></p> <p>(74) Agents: <b>BROOK, David, E. et al.; Hamilton, Brook, Smith &amp; Reynolds, Two Militia Drive, Lexington, MA 02173 (US).</b></p>		<p>(81) Designated States: <b>AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LÜ, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</b></p> <p><b>Published</b>  <i>With international search report.  Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: <b>APPARATUS AND METHOD FOR APPLYING A PARTICULATE HEMOSTATIC AGENT TO LIVING TISSUE</b></p>		
<p>(57) Abstract</p> <p>An apparatus and method for applying a particulate hemostatic agent to living tissue are disclosed. The apparatus includes a particulate hemostatic agent source (22) and a continuous gas source (14). A continuous gas stream from the continuous gas source is turbulently combined with the particulate hemostatic agent within the hemostatic agent source to form a finely dispersed fluid stream of the particulate hemostatic agent in the continuous gas stream. An outlet conduit (34) extends from where the gas and particulate hemostatic agent are combined through an outlet (36) of the conduit, whereby the fluid stream is conducted through the outlet conduit and is discharged from the outlet conduit onto proximate living tissue, thereby applying the particulate hemostatic agent to the living tissue.</p>		

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APPARATUS AND METHOD FOR APPLYING A PARTICULATE  
HEMOSTATIC AGENT TO LIVING TISSUE

Background of the Invention

After tissue has been wounded or cut, the opening  
5 must be surgically closed to stop bleeding and enable  
healing of the tissue. In cases of severe wounds and  
skin grafting, an insufficient amount of tissue can  
exist around the sides of the wound or surgical  
incision to allow the sides to be pulled together.  
10 Similarly, when diseased or blemished tissue is removed  
by surgery, insufficient tissue may be left around the  
perimeter of the removed tissue. These procedures are  
invasive and have substantial risks of complications,  
including that of infection.

15 One attempt to stem blood loss and to facilitate  
wound closure is application of a hemostatic agent,  
such as collagen, to the wound to form a wound  
dressing. The hemostatic agent, on contact with blood  
or other body fluids, adheres to the tissue and stems  
20 bleeding.

However, hemostatic agents are extremely  
hydrophilic. Upon contact with moisture from the wound  
or the atmosphere, the fibrillar hemostats have a  
tendency to clump and adhere tenaciously to any object.  
25 These objects include instruments, gloves, non-bleeding  
tissues and other surfaces in addition to the intended  
open wound or surgical incision. This clumping and  
adhesion makes application of the hemostatic agent to  
the wound difficult.

-2-

Summary of the Invention

The present invention relates to an apparatus and method for applying a particulate hemostatic agent to living tissue.

5       The apparatus includes a particulate hemostatic agent source, a continuous gas source and means for combining a turbulent continuous gas stream from the gas source with the particulate hemostatic agent within the hemostat agent source to form a finely dispersed  
10 fluid stream of the particulate hemostatic agent in the gas. The apparatus further includes an outlet conduit extending from means for combining the gas and particulate hemostatic agent through an outlet of the  
15 the outlet conduit and is discharged from the outlet conduit onto proximate living tissue, thereby applying the particulate hemostatic agent to the living tissue.

      The method includes the steps of combining a turbulent continuous gas stream with the particulate  
20 hemostatic agent to form a finely dispersed fluid stream of the particulate hemostatic agent in the gas. The fluid stream is directed through an outlet conduit, whereby the fluid stream is conducted through the outlet conduit and onto proximate living tissue,  
25 thereby applying the particulate hemostatic agent to the living tissue.

-3-

This invention has many advantages which include an apparatus that allows accurate placement by a surgeon of the particulate hemostatic agent onto a bleeding site. The apparatus is easy to hold and to use, and it allows the surgeon to view the placement of the particulate hemostatic agent on the tissue. By forming a finely dispersed fluid stream of the hemostatic agent in a turbulent continuous gas stream, the apparatus minimizes the problem of sticking or clumping before reaching the targeted wound or surgical incision and allows for control of the amount of particulate hemostatic agent applied.

#### Brief Description of the Drawings

Figure 1 is an orthogonal projection side view of one embodiment of the apparatus of the present invention.

Figure 2 is an orthogonal projection end view of the embodiment shown in Figure 1.

Figure 3 is a second embodiment of the apparatus of the present invention.

Figure 4 is an orthogonal projection side view of a third embodiment of the apparatus of the present invention.

Figure 5 is an orthogonal projection end view of the third embodiment shown in Figure 3 taken along line III-III.

-4-

Detailed Description of the Invention

The features and other details of the method and apparatus of the invention will now be more particularly described with reference to the accompanying drawings and pointed out in the claims. The same numeral present in different figures represents the same item. It will be understood that the particular embodiments of the invention are shown by way of illustration and not as limitations of the invention. The principle features of this invention can be employed in various embodiments without departing from the scope of the invention.

One embodiment of the invention, as shown in Figure 1, a side view, and in Figure 2, an end view, is spray device 10, which can be a hand held device. As can be seen in Figure 1, spray device 10 has gas inlet 12 for receiving a continuous gas stream from continuous gas source 14 through gas tube 16. A continuous gas stream is considered one that can be maintained without interruption or cessation for an extended period of time, although the flow rates can be varied over the period of time. Gas tube 16 is flexible and sufficiently resilient to direct a continuous gas stream at a velocity of between about 20 and 200 cm/sec. The flow of continuous gas stream can be controlled by valve 15. In one embodiment, valve 15 is activated by a floor mounted pedal switch which can be operated by a surgeon using his foot.

-5-

A suitable gas is one that can form a fluid stream of particulate hemostatic agent by combination with a particulate hemostatic agent. In one embodiment, the gas is substantially inert in the presence of the  
5 particulate hemostatic agent and living tissue. Example of such gases include air, nitrogen, helium, argon, carbon dioxide, etc., or a combination thereof. These gases should be sterile because they come in contact with the open wound or surgical incision in the  
10 living tissue. Further, the gas has a low-humidity content because suitable particulate hemostatic agents generally have a tendency to clump when exposed to moisture. Typically, the gas has a relative humidity of less than about thirty percent.

15 Spray device 10 has handle 18 and nozzle 20. Handle 18 can be sized so as to be easily held with one hand. Handle 18 can be made of metal or other material which would readily allow a secure grip by the surgeon or operator of the device. Gas inlet passage 21 is  
20 disposed within handle 18 for receiving the continuous gas stream from gas tube 16 and directing the gas through particulate hemostatic agent source gas inlet 24 to particulate hemostatic agent source 22 to form a fluid stream of the particulate hemostatic agent in the  
25 gas.

A wide variety of particulate hemostatic agents can be used with this invention. For example, the particulate hemostatic agent can include cellular  
fibers which act as chemical agents to stop bleeding of  
30 living tissue. Examples of a suitable particulate hemostatic agent include collagen, nonsoluble

-6-

polysaccharide, cellulose and dried gelatin. Collagen can be obtained from many mammalian sources, such as from the hides of cows, pigs, sheep, goats, etc., and can be denatured. The particulate hemostatic agent can be in the form of fibers, powder, flakes, particles, milled fibrillar particles, etc. which can readily form of fluid stream in a continuous gas stream for transporting and dispersing the hemostatic agent. Generally, the density of the hemostatic agent is in the range of between about one and four pounds/ft<sup>3</sup> (0.016-0.064 g/cm<sup>3</sup>). A particularly suitable collagen hemostatic agent is commercially available as Avitene<sup>®</sup> fibrillar hemostatic agent, from MedChem Products, Inc., Woburn, Massachusetts. Another hemostatic agent is a gelatin powder commercially available under the trademark of Gelfoam<sup>®</sup> from Upjohn Corporation.

As can be seen in Figure 2, particulate hemostatic agent source 22 is attached to spray device 10 by suitable means, such as screw threads 26 or by other means, such as a clamp, etc. Particulate hemostatic agent source 22 has source chamber 28 for containing the hemostatic agent. In one embodiment, the amount of particulate hemostatic agent in particulate hemostatic agent source 22 is about one gram. The interior of source chamber 28 is shaped to allow the entering gas to mix sufficiently with the particulate hemostatic agent to break up and disperse any agglomeration of hemostatic agent and to form a finely dispersed fluid suspension within chamber 28. The suspension is directed from particulate hemostatic agent source 22 through particulate hemostatic agent source outlet 30



-7-

to form a turbulent fluid stream of particulate hemostatic agent. In one embodiment, source chamber 28 has curved corners 32 to direct the gas within source chamber 28, thereby assisting in directing the  
5 continuous gas stream to combine with the particulate hemostatic agent and form a fluid stream therewith.

Turbine means 25 which is held in place by support 23 can be placed within particulate hemostatic agent source 22 to allow the formed fluid stream to be more  
10 finely dispersed. Turbine means 25 is propelled by the continuous gas stream as it is directed through particulate hemostatic agent source 22. Rotation of turbine means 25 substantially prevents agglomeration of particulate hemostatic agent in source 22 while the  
15 gas stream is being directed through source 22.

Returning to Figure 1, nozzle 20 has interior conduit 34, which extends from particulate hemostatic agent source 22 to conduit outlet 36. Preferably, interior conduit 34 has a substantially constant  
20 internal diameter along the length of nozzle 20 through outlet 36. Also, conduit outlet 36 has the same shape and size of the cross section of interior conduit 34. In one embodiment, nozzle 20 is about twenty centimeters long, and conduit 34 and conduit outlet 36  
25 both have a diameter of about 1.25 centimeters.

The continuous gas stream is directed from continuous gas source 14 through gas tube 16 to gas inlet 12 of gas inlet passage 21 of spray device 10. In one embodiment, a gas, such as dry nitrogen gas, is  
30 directed at a velocity of between about 20 and 200 cm/sec. The continuous gas stream is directed from gas

-8-

inlet passage 21 through particulate hemostatic agent source inlet 24 to particulate hemostatic agent source 22.

Particulate hemostatic agent source 22 has  
5 particles of hemostatic agent which are sufficiently small to allow the directed gas to form a fluid stream. The particulate hemostatic agent and the continuous gas stream are mixed sufficiently within particulate  
10 hemostatic agent source 22 to form a fluid stream of particulate hemostatic agent in the gas. The fluid stream is directed from particulate hemostatic agent outlet 30 through interior conduit 34. The particulate hemostatic agent is then directed from conduit outlet  
15 36 onto a proximate wound or incision. Conduit outlet 36 is positioned proximate to the surface of the tissue so that the fluid stream can be spread over the wound or incision, thereby forming a layer of particulate hemostatic agent.

Another embodiment of the invention, as shown in  
20 Figure 3, is a spraying device 50, which can be a hand held device and is portable. As can be seen in Figure 3, spraying device 50 has gas inlet tube 52 for receiving a continuous gas stream from gas source 54. The flow of continuous gas stream can be controlled by  
25 valve 56. In one embodiment, valve 56 is activated by a hand-pushed button.

Spraying device 50 has handle 58 and nozzle 60. Gas inlet passage 62 is disposed within spraying device 50 for receiving the continuous gas stream from gas  
30 tube 52 and directing the gas through particulate hemostatic agent source gas inlet 64 to particulate

-9-

hemostatic agent source 66 which has particulate hemostatic agent chamber 68 for containing the hemostatic agent to form a fluid stream of the particulate hemostatic agent in the gas. Particulate hemostatic agent source gas inlet 64 has inlet conduits 5 70,72. First inlet conduit 70 allows a jet of gas to enter particulate hemostatic agent chamber 68 and mix with the particulate hemostatic agent to provide a continuous supply of suspended hemostatic agent by causing turbulent agitation of the agent inside 10 particulate hemostatic agent chamber 68 thereby forming a dispersed fluid suspension of particulates within chamber 68. In a preferred embodiment, first inlet conduit 70 directs the jet of gas helically into 15 particulate hemostatic agent chamber 68. Second inlet conduit 72 is sufficiently proximate to particulate hemostatic chamber outlet 74 to allow the gas entering particulate hemostatic agent chamber 68 to break up and disperse throughout chamber 68 any agglomeration of 20 particulate hemostatic agent that would otherwise block particulate hemostatic chamber outlet 74 while the gas stream is directed through particulate hemostatic agent source 66, thereby allowing the particulate hemostatic agent to be discharged through particulate hemostatic 25 chamber outlet 74 as a finely dispersed fluid stream. Particulate hemostatic agent chamber gas inlet 64 is not necessarily limited to the exemplified two conduits. For instance, gas inlet 64 can have a plurality of conduits distributed through the top of 30 particulate hemostatic agent chamber 68 with at least

-10-

one conduit proximate to particulate hemostatic chamber outlet 74.

Particulate hemostatic agent chamber 74 is attached to spraying device 50 by suitable means, such as threads 76. The interior of particulate hemostatic agent chamber 68 is shaped to allow the entering gas to mix sufficiently with the particulate hemostatic agent to form a fluid stream of particulate hemostatic agent source 66 through particulate hemostatic chamber outlet 74, thereby forming a fluid stream of particulate hemostatic agent.

Nozzle 60 has interior conduit 78, which extends from particulate hemostatic agent source 66 to conduit outlet 80. Conduit outlet 80 has the same shape and size of the cross section of interior conduit 78. In one embodiment, nozzle 60 is about eight centimeters long and interior conduit 78 and conduit outlet 80 both have a diameter of about 0.5 centimeters.

Another embodiment of the invention, as shown in Figure 4, a side view, and in Figure 5, which is an end view taken along line III-III of Figure 4, is spray apparatus 100. As can be seen in Figure 4, spray apparatus 100 includes cylinder 102. Cylinder 102 has interior passage 104 which has a substantially constant internal diameter the length of cylinder 102 through outlet 106. In other words, the diameter of outlet 106 is about the same as that of interior passage 104. Cylinder 102 is suitable for holding particulate hemostatic agent 105 therein.

-11-

Opening 108 at end 109 is configured for receiving  
slidable valve gate 110. Valve gate 110 is  
sufficiently sized and shaped to slide along the  
interior of cylinder 102 through second opening 108  
5 while not allowing a significant amount of gas to pass  
between cylinder 102 and valve gate 110. As shown in  
Figure 5, valve gate 110 is held in place by  
protrusions 121 within interior passage 104 of cylinder  
102.

10       Returning to Figure 4, inlets 112, 114, 116, 118,  
120 can be of constant or varying cross-sectional area.  
Alternatively, the inlet can be a slot which extends  
along the conduit. Inlets 112, 114, 116, 118, 120 have  
a sufficient diameter to allow a gas to pass through  
15 the inlets and enter cylinder 102.

The flow of gas from continuous gas source 111  
through tube 115 to gas distributor 122 is controlled  
by valve 113 which can be activated by a floor mounted  
pedal switch. Gas distributor 122 is placed  
20 substantially along the length of cylinder 102 and has  
a plurality of outlets that allows the gas stream to  
form a plurality of streams through gas inlets 112,  
114, 116, 118, 120.

Spraying apparatus 100 is operated by sliding  
25 valve gate 110 in direction 136 along the interior of  
cylinder 102 to thereby successively open gas inlets  
112, 114, 116, 118, 120. To close gas inlets 112, 114,  
116, 118, 120, valve gate 110 is closed by sliding in  
direction 134. For example, as gas inlet 112 is  
30 opened, gas is directed through the inlet into cylinder  
102, thereby displacing particulate hemostatic agent in

-12-

cylinder 102 between the opening and outlet 106. The displaced particulated hemostatic agent is consequentially directed out of cylinder 102 through outlet 106 and onto proximate tissue. When at least a substantial portion of the hemostatic agent has been discharged from between gas inlet 112 and outlet 106, slide valve gate 106 is further retracted to open gas inlet 114. Hemostatic agent in cylinder 102 between gas inlets 112 and 114 is thereby displaced. The hemostatic agent is consequently directed by the gas stream out of cylinder 102 through outlet 106 onto the proximate tissue. As each successive gas inlet is opened by sliding movement of valve gate 110, the particulate hemostatic agent is controllably discharged from apparatus 100, thereby forming a layer of the particulate hemostatic agent on a proximate wound or incision, thereby stemming bleeding and facilitating tissue closure.

Spraying apparatus 100 is composed of materials that can be easily cleaned and sterilized, such as stainless steel. The components of spraying apparatus 100 are easily disassembled to remove any particulate hemostatic agent deposited within the interior of spraying apparatus.

The amount of particulate hemostatic agent directed onto a wound or incision is dependent on the concentration of particulate hemostatic agent in the fluid stream. For example, the concentration can be about thirty grams per liter. The gas velocity can be in the range of between about twenty and two hundred centimeters per second.

-13-

Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific  
5 embodiments of the invention described specifically herein. Such equivalents are intended to be encompassed in the scope of the claims.

-14-

CLAIMS

1. An apparatus for applying a particulate hemostatic agent to living tissue, comprising:
  - a) a particulate hemostatic agent source;
  - b) a continuous gas source;
  - c) means for combining a turbulent continuous gas stream from the gas source with the particulate hemostatic agent within the hemostatic agent source to form a finely dispersed fluid stream of said particulate hemostatic agent in said gas; and
  - d) an outlet conduit extending from said means for combining the gas and particulate hemostatic agent, whereby said fluid stream is conducted through the outlet conduit and is discharged from the outlet conduit onto proximate living tissue, thereby applying the particulate hemostatic agent to the living tissue.
2. An apparatus of Claim 1 wherein said particulate hemostatic agent source is within said outlet conduit and wherein said outlet conduit has at least one inlet which extends along the length of the conduit, whereby the particulate hemostatic agent extends between the inlet and the outlet of the conduit.



-15-

3. An apparatus of Claim 2 wherein the means for combining the continuous gas stream with the particulate hemostatic agent to form the fluid stream includes a valve at the inlet of the outlet conduit for controlling the rate and location along the outlet conduit through which the gas flows into the conduit.
4. An apparatus of Claim 3 wherein the valve is a sliding gate valve which extends along the conduit, whereby the gas is directed to the particulate hemostatic agent packed within the conduit by sliding said valve along the outlet conduit.
5. An apparatus of Claim 4 wherein the inlet is a slot which extends along the outlet conduit.
6. An apparatus of Claim 4 wherein a plurality of inlets extend along the outlet conduit.
7. An apparatus of Claim 1 wherein the means for combining the continuous gas stream with the particulate hemostatic agent to form a fluid stream includes an inlet conduit which extends from the continuous gas source to the particulate hemostatic agent source.

-16-

8. An apparatus of Claim 7 further including means for agitating the particulate hemostatic agent at the hemostatic agent source while the continuous gas stream is being directed through the hemostatic agent source.
9. An apparatus of Claim 8 wherein the means for agitating the particulate hemostatic agent includes a turbine which is propelled by the continuous gas stream directed through the hemostatic agent source.
10. An apparatus of Claim 9 further including means for controlling the rate of flow of the continuous gas through the hemostatic agent source.
11. An apparatus of Claim 1 wherein the particulate hemostatic agent source includes a plurality of gas inlets for receiving the gas from said continuous gas source, whereby at least one gas inlet directs the gas into said source to cause entering gas to agitate and disperse said hemostatic agent.
12. An apparatus of Claim 11 wherein the particulate hemostatic agent source further includes at least one of said gas inlets which is proximate to said conduit extending from said hemostatic agent source chamber outlet to cause entering gas to disperse agglomerated hemostatic agent within said hemostatic agent source.

-17-

13. A method for applying a particulate hemostatic agent to living tissue, comprising the steps of:
  - a) combining a turbulent continuous gas stream with the particulate hemostatic agent to form a finely dispersed fluid stream of said particulate hemostatic agent in said gas; and
  - b) directing the finely dispersed fluid stream through an outlet conduit having a substantially constant internal diameter, whereby said fluid stream is conducted through the outlet conduit and onto proximate living tissue, thereby applying the particulate hemostatic agent to the living tissue.
14. A method of Claim 13 wherein the particulate hemostatic agent is cellulose.
15. A method of Claim 13 wherein the particulate hemostatic agent is a non-soluble polysaccharide.
16. A method of Claim 13 wherein the particulate hemostatic agent is collagen.
17. A method of Claim 16 wherein the collagen is substantially denatured.
18. A method of Claim 17 wherein the collagen is in the form of flakes.

-18-

19. A method of Claim 17 wherein the collagen is in the form of a powder.
20. A method of Claim 16 wherein the collagen is in the form of milled fibrillar particles.
21. A method of Claim 20 wherein the gas is selected from the group consisting of air, nitrogen, carbon dioxide, helium and argon.
22. An apparatus for applying a particulate hemostatic agent to living tissue, comprising:
  - a) a continuous gas source;
  - b) an elongate outlet conduit having at least one inlet which extends along the length of the elongate outlet conduit, said elongate outlet conduit also having a substantially constant internal diameter through the conduit to an outlet of said conduit;
  - c) a particulate hemostatic agent packed within the elongate outlet conduit and extending between the inlet and the outlet of the elongate outlet conduit; and
  - d) a valve at the inlet for controlling the rate and location along the elongate outlet conduit through which the gas flows into said conduit, whereby the gas combines with the particulate hemostatic agent to form a finely dispersed fluid stream of said particulate hemostatic agent in said gas, said fluid stream being conducted through the outlet and

-19-

onto proximate living tissue, thereby applying the particulate hemostatic agent to said living tissue.

23. An apparatus of Claim 22 wherein the valve is a slidable gate which extends along the elongate outlet conduit, whereby the gas is directed to the particulate hemostatic agent packed within the elongate outlet conduit by sliding said slidable gate along said conduit.
24. An apparatus for applying a particulate hemostatic agent to living tissue, comprising:
  - a) a particulate hemostatic agent source;
  - b) a turbulent continuous gas source;
  - c) means for directing gas from the continuous gas source through the particulate hemostatic agent source, whereby a finely dispersed fluid stream of the particulate hemostatic agent and the gas is formed; and
  - d) an elongate outlet conduit extending from the particulate hemostatic agent source, said elongate conduit having a substantially constant internal diameter through an outlet of said elongate outlet conduit.
25. An apparatus of Claim 24 further including means for agitating the particulate hemostatic agent in the particulate hemostatic agent source during direction of the gas through said particulate hemostatic agent source.

-20-

26. An apparatus of Claim 25 wherein the particulate hemostatic agent source includes a plurality of gas inlets for receiving the gas from said continuous gas source, whereby at least one gas inlet directs the gas into said source to cause entering gas to agitate and disperse said hemostatic agent.
27. An apparatus of claim 26 wherein the particulate hemostatic agent source further includes at least one of said gas inlets which is proximate to said conduit extending from said hemostatic agent source chamber outlet to cause entering gas to disperse agglomerated hemostatic agent within said hemostatic agent source.

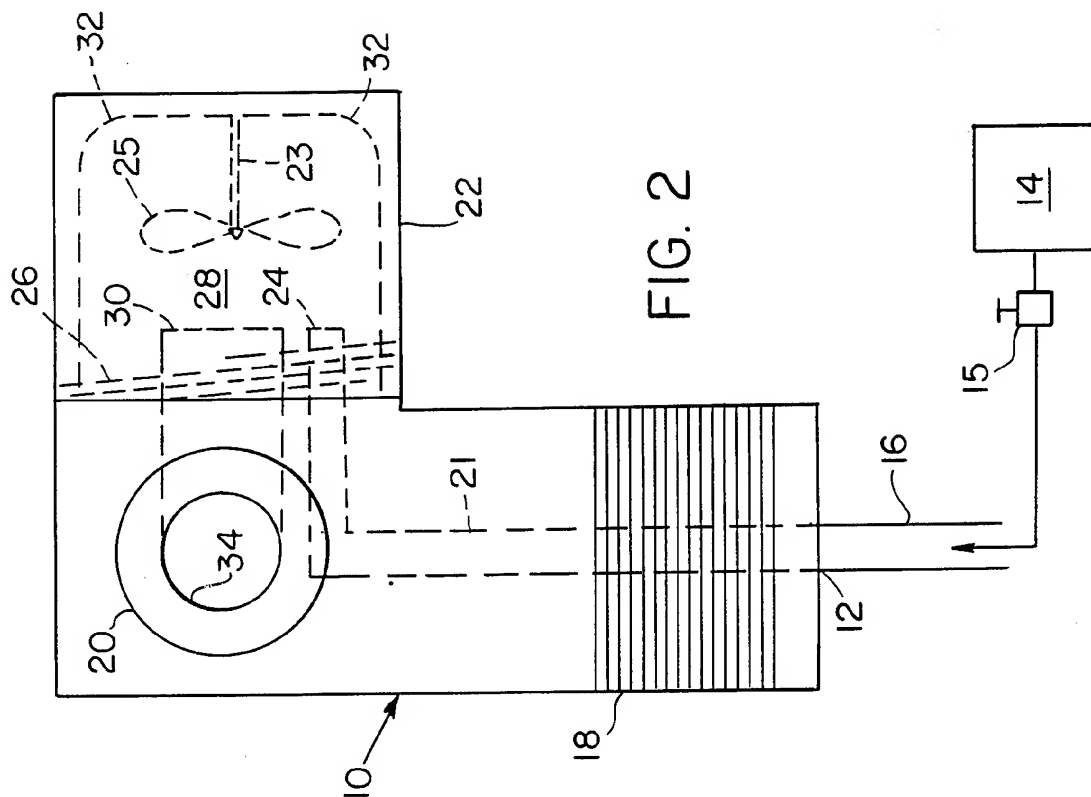


FIG. 2

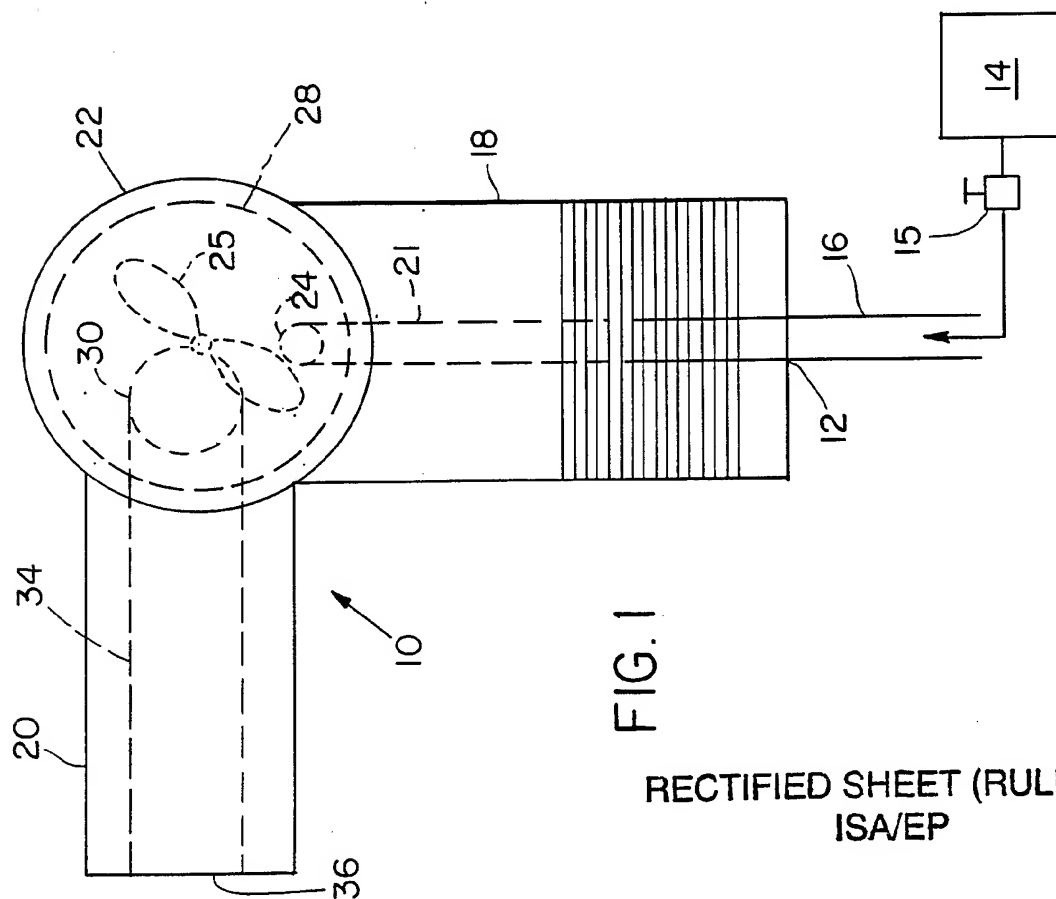


FIG. 1

2/2

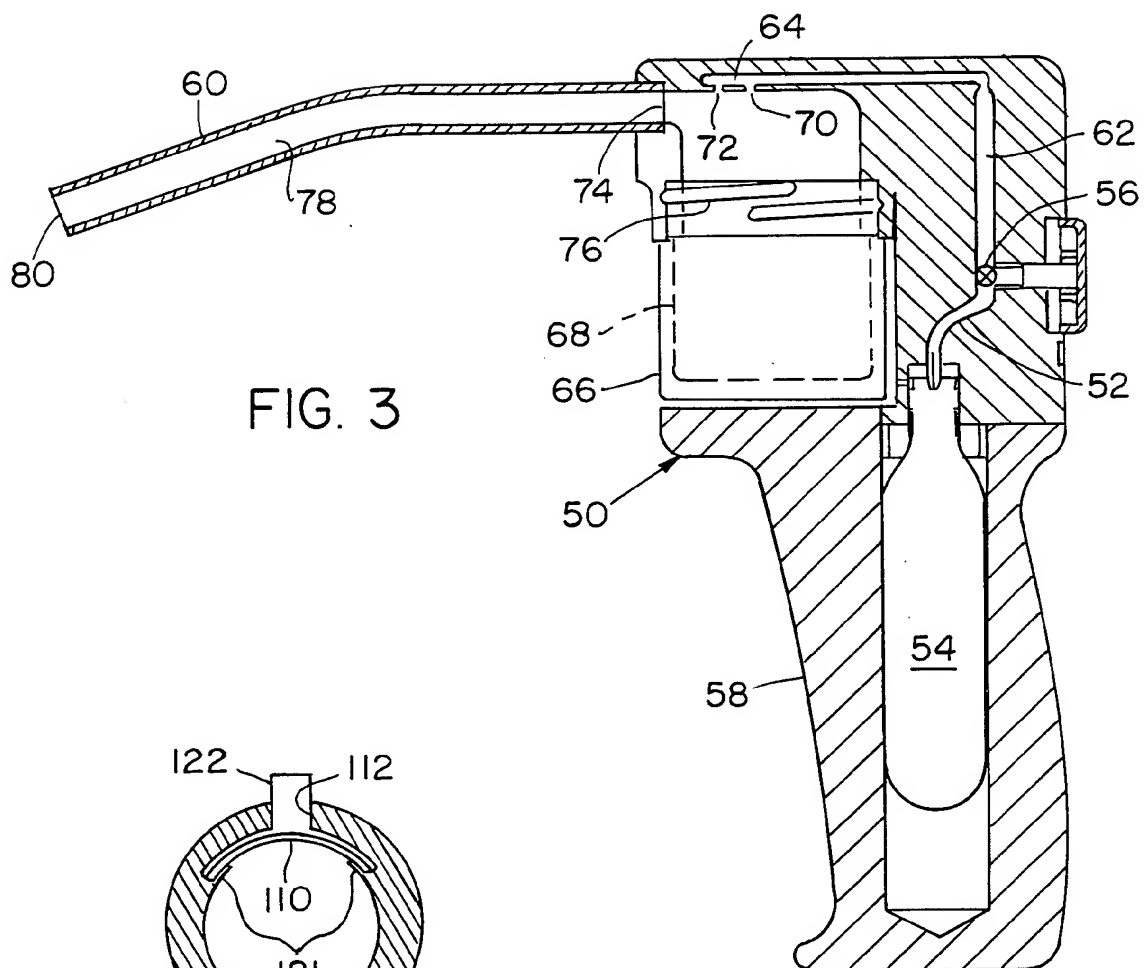


FIG. 3

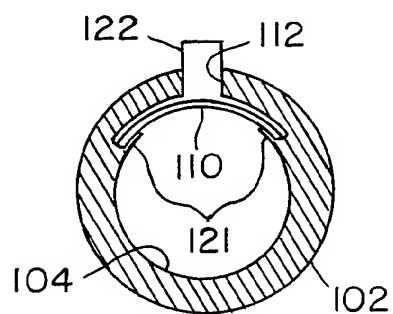


FIG. 5

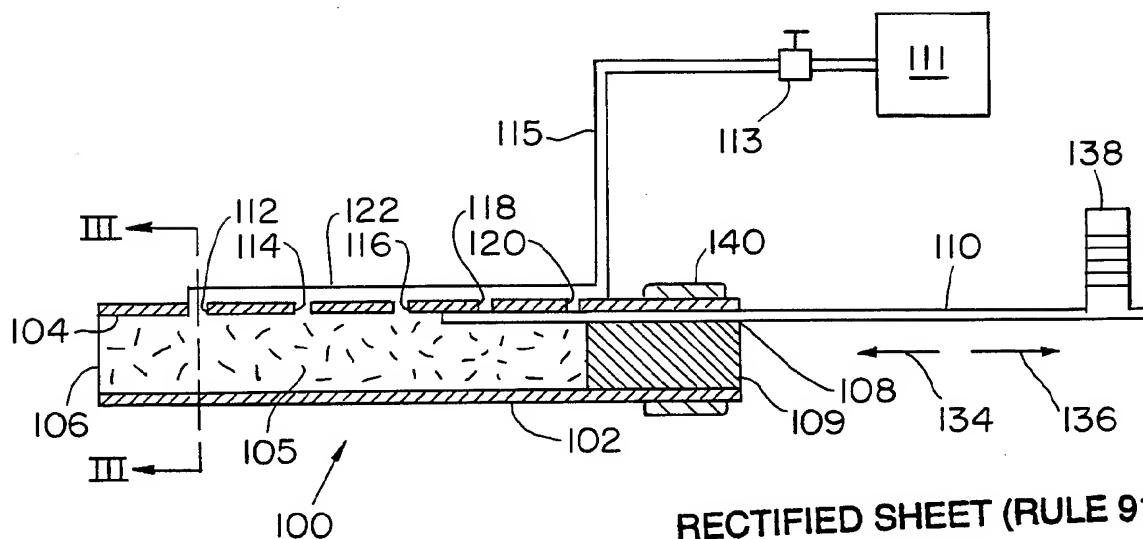


FIG. 4

RECTIFIED SHEET (RULE 91)  
ISA/EP



# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 94/04193

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 5 A61M35/00 A61M11/02

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 5 A61M B05B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US,A,4 204 645 (HOPP) 27 May 1980	1-3,7, 22,24
Y	* THE WHOLE DOCUMENT *	4-6, 8-12,23, 25-27
Y	<p>---                      DATABASE WPI                      Week 8340,                      Derwent Publications Ltd., London, GB;                      AN 83-781541                      &amp; SU,A,978 999 (SINYAKEVICH ET AL.)                      see abstract                      ---                      -/--</p>	4-6,23

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

22 July 1994

Date of mailing of the international search report

(23.08.94)

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# INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US,H,257 (BARDITCH ET AL.) 7 April 1987  see abstract see column 1, line 43 - column 2, line 46 see column 3, line 35 - column 4, line 31 ---	8-12, 25-27
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